

AMENDMENTS TO THE SPECIFICATION

1. Amend the paragraph beginning at page 3, line 6, as shown below:

The artificial tissue of the invention displays one or more characteristics of natural tissue. For example, the artificial tissue produces one or more compounds selected from the group consisting of laminin, fibronectin, collagen I, collagen III, hyaluronic acid, VEGF 145, VEGF 121, bFGF, IL-8, Syndecan-1, CXCR-1, CXCR-2, a mannose-containing protein, an acetylglucosamine-containing protein, PECAM-1, alpha-SMA, MMP-2, a growth factor receptor, plasminogen activator, mSRA, and CD68. In another embodiment, the microvessels of the artificial tissue produce one or more blood cells. In a preferred embodiment, the microvessels of artificial tissue produces one or more mononuclear leukocytes. In another embodiment, the artificial tissue produces one or more periendothelial ~~perioendothelial~~ cells. In a further embodiment, the artificial tissue produces an extracellular matrix. In yet a further embodiment, the artificial tissue is self-maintained.

2. Amend the paragraph beginning at page 4, line 3, as shown below:

Figure 2 is a set of optical microscope pictures of three-dimensional culture cross sections, illustrating microvessels with lumen and periendothelial ~~perioendothelial~~ cells. Figure 2A is a section through a multilayered epithelium. Figure 2B is a section through microvessels surrounded by numerous fibroblasts.

3. Amend the paragraph beginning at page 4, line 27, as shown below:

The artificial tissue forms one or more microvessels with a continuous basal lamina; this is an advantage of the invention. In various embodiments, these microvessels are characterized by any of a variety of structures and/or biochemical markers, e.g., the presence of periendothelial ~~perioendothelial~~ cells, the presence of blood cells, the presence of endothelial cell specific proteins.

4. Amend the paragraph beginning at page 5, line 16, as shown below:

A "primary cell" is a cell taken ~~directly~~ from a living organism, which cell is not immortalized.

5. Amend the paragraph beginning at page 6, line 30, as shown below:

The term "periendothelial ~~perioendothelial~~ cells" refers to cells with one or more characteristics of periendothelial ~~perioendothelial~~ cells. These characteristics are well-known to one of skill in the art and may be morphological, physiological or biochemical. One example of said characteristics is expression of alpha smooth muscle actin (alpha-SMA).

6. Amend the paragraph beginning at page 11, line 5, as shown below:

For example, one or more microvessels are produced in the artificial tissue of the invention. The microvessels are generally composed of a tight monolayer of endothelial cells surrounding a lumen. In one embodiment, the microvessels are contacted by sparse periendothelial ~~perioendothelial~~ cells as observed by, e.g., optical microscopy. The periendothelial ~~perioendothelial~~ can also be identified by cell specific markers. In one embodiment the periendothelial ~~perioendothelial~~ cells are identified by the cell specific marker alpha-smooth muscle actin (alpha-SMA) using immunolabelling with alpha-SMA specific antibodies and confocal microscopy.

7. Amend the paragraph beginning at page 18, line 17, as shown below:

The most common process by which new blood vessels form in adults occurs by sprouting from pre-existing vessels (angiogenesis). This process can be productively divided into the following steps: (1) Destabilization of endothelium, leading to blood vessel permeability and flexibility; (2) degradation of the basal lamina that surrounds the preexisting blood vessels; (3) localized proliferation of endothelial cells to provide cells for sprout formation; (4) endothelial cell migration, tube formation and elongation of the sprout; (5) stabilization of the endothelium by deposition of new basal lamina; (6) recruitment of ~~perioendothelial~~ support cells to the endothelium; (7) stabilization of the interactions between periendothelial ~~perioendothelial~~ cells and endothelial cells; and (8) formation of mature microvessels. Numerous factors have been identified that participate in these steps of sprout formation during embryonic development. However, in adults, angiogenesis driven by injury or pathological conditions involves additional/alternative factors, including chemokines, of which IL-8 is a major player (e.g. Arenberg et al., 1997a & b).

8. Amend the Abstract of the Disclosure as shown below:

An in vitro, three dimensional artificial tissue that resembles human skin has been developed. Microvascular endothelial cells from human adult lung were sandwiched between two layers of human dermal fibroblasts in three dimensional collagen gels. The sandwich was covered with keratinocytes. The cultures were self-maintained for prolonged periods of time without the addition of tumor promoters such as phorbol esters. Over a few days, the keratinocytes developed into a multilayered epithelium. Microvessels were produced in the support matrix. The microvessels were composed of a tight monolayer of endothelial cells surrounded by a continuous basal lamina, contacted by newly formed, sparse periendothelial ~~perioendothelial~~ cells. The microvessels also contained newly formed blood cells. Human matrix molecules characteristic of skin were produced. This artificial tissue is an in vitro system that closely resembles human skin, and provides both a powerful model to study cellular and molecular mechanisms involved in skin development and replacement and a basis for a new generation skin replacement product.